

REMARKS

Applicant has amended claim 11 line 2 of step (e) has replace the term "fragment" with the term "fragments" as requested by the Examiner.

In claim 20 Applicant has added an additional step providing "modulating at least one cell or at least one nucleus" prior to the cross-linking step to more particularly point out and distinctly claim Applicant's invention.

In claim 23 Applicant has removed the repeated term "isolated" in the first line to avoid confusion.

In claim 24 Applicant has amended the claim replacing "49" with "20" to provide the correct claim dependency.

In claim 29 Applicant has amended claim 29 replacing "22" with "20" to provide the correct claim dependency.

In addition Applicant has added new claims 32-38 to more particularly point out and distinctly claim Applicant's invention. Support for these new claims may be found throughout the specification and more particularly on pages page 31, line 13 to page 33 line 12 for discussion of arrays, page 15, lines 1-6 and page 30 lines 1-3 for discussion of modulating and example of modulating conditions and figures 2 and 3 showing the comparing step of modulated versus non-modulated expression.

To the best of their knowledge Applicant's believe that the amendments to the specification do not add new matter.

PATENTABILITY ARGUMENTS

A. Response to 35 U.S.C. §102 (b) Rejections

In item 7 of the detailed action, the Examiner rejects claims 1-10 and 20-29 as being anticipated by de Belle *et al.* (Biotechniques 29:162, July 2000). Claims 1-10 has been cancelled consequently this rejection is moot. For the Examiner to maintain a rejection under 35 U.S.C. §102 every element of Applicant's invention must be taught by the cited reference. Regarding claims 20-29, Application has amended the specification to include a section titled "Reference to Related Applications". This sections states that "(T)his application is a continuation-in-part of patent application serial no.: 09/270,391 filed 16 March 1999 now patent no.: 6,410,233." Since this application was pending at the time the present application was filed, the requirement that both applications be copending to obtain

the priority date of the parent application has been met. Consequently rejections based on 35 U.S.C. §102(b) in view of de Belle *et al.* are moot since the application now maintains priority to 16 March 1999 which was more than one year prior to the publication of de Belle *et al.* In addition, authors of the cited reference, Daniel Mercola, Eileen Adamson and Ian de Belle are the inventors of record regarding the methods claimed in the current application.

In item 8, the Examiner further rejects claims 2, 3, 6, 7, 9, 10, 20, 22, 23, 26, 27 and 29 as being anticipated by Orlando *et al.* (Cell 75:1187, 1993). Claims 2, 3, 6, 7, 9, and 10 have been cancelled consequently this rejection is moot. Claim 20 has been amended to include the limitation that the at least one cell or at least one nucleus has been stimulated with radiation. As stated by the Examiner Orlando *et al.* does not teach a step of stimulating at least one cell or nucleus with radiation consequently a rejection under 35 USC §102(b) cannot be maintained. Since claims 21, 22, 23, 26, 27 and 29 all depend from claim 20 rejections under 35 U.S.C. §102(b) also cannot be maintained and Applicant's respectfully requests that the Examiner remove these rejections.

B. Response to 35 U.S.C. §103 (a) Rejections

In item 11 the Examiner rejects claims 1, 4, 5, 8, 24, 25 and 28 as being unpatentable over Orlando *et al.* in view of Hallahan *et al.* (The Journal of Biological Chemistry 270:30303, 1995). Applicants respectfully disagree. In order for the Examiner to maintain a rejection under 35 U.S.C. §103(a) there must be some motivation to combine the teachings of the cited references, there must be a reasonable expectation of success when combining the teachings of the references and the references must teach or suggest all of the claim limitations. Claims 1, 4, 5, 8 and 28 have been cancelled consequently this rejection is moot.

Claim 28 has been canceled because of its incorporation into claim 20. In view of this Applicant's will address the 35 U.S.C. §103(a) rejection of claim 28 for claim 20 as well as for claims 24 and 25. The Examiner states that it would have been *prima facie* obvious for one skilled in the art at the time the invention was made to have modified the methods of Orlando *et al.* to incorporate the step of exposing cells to ionizing radiation for the induction of transcription factor EGR-1. Next the Examiner states that one skilled in the art would be motivated to modify the teaching of Orlando, *et al.* to include the application of ionizing radiation prior to cross-linking to induce production of EGR-1 transcription factor for study. Applicants respectfully disagree.

First, it is important to note that Orlando *et al.* is looking to identify REPRESSED-DOMAINS OF KNOWN GENES repressed by polycomb and Hallahan is looking for the EFFECT OF IONIZING RADIATION ON DNA SYNTHESIS AND CELL SURVIVAL.

Applicants are doing neither therefore one skilled in the art would not be motivated to combine these references.

Second, Applicant's are looking at ACTIVATED DOMAINS NOT REPRESSED DOMAINS consequently one skilled in the art would not look to the teachings of Orlando, *et al.* to obtain any meaningful methods that would allow the study of active domains. Therefore one skilled in the art would not be motivated to combine these references.

Third, Applicant's are looking for useful information for HUMAN APPLICATION. One skilled in the art would not look to methods used for insect cell lines when conducting experiments on human cell lines because the cells are substantially different in physiology and would not provide meaningful information for human application. Therefore one skilled in the art would not be motivated to combine these references.

Fourth, the methods of Orlando *et al.* are focused on mapping of polycomb-repressed domains that are located in tightly wound chromatin. It is known in the art that transcription factor EGR-1 binds to active domains which comprise unwound or open chromatin, therefore, it would be NOT be obvious for one skilled in the art to look to the teachings of Orlando *et al.* for the identification of *in vivo* target genes of the transcription factor EGR-1. More specifically, one skilled in the art would not modify the teachings of Orlando *et al.* because one would recognize that EGR-1 would not bind to tightly wound chromatin or provide any meaningful data on identification of *in vivo* target genes of the transcription factor EGR-1. Therefore one skilled in the art would not expect to have a reasonable chance of success when combining these references without undue experimentation.

Fifth, Ionizing radiation causes damage to double stranded DNA and correspondingly can damage EGR-1 stress activated sites, adding this step to the teachings of Orlando, *et al.* could activate some repressed domains but would not provide any useful information on mapping the polycomb-repressed domains. More specifically one skilled in the art would not expect useful results by modifying the methods of Orlando *et al.* to include an ionizing radiation step because fragmenting double stranded DNA in tightly wound chromatin frustrates the intent of obtaining information on repressed-domains. Therefore one skilled in the art would not expect to have a reasonable chance of success when combining these references without undue experimentation.

In view of the above arguments Applicants respectfully request that the Examiner remove this rejection.

C. Response to Double Patenting Rejection

The Examiner rejects claims 1-29 under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1 through 9 of U.S. patent 6,410,233. Applicant's respectfully disagree. However, the specification has been amended to include the section titled "Reference to Related Applications" stating that this application is a continuation-in-part from patent no.: 6,410,233, which maintains the priority of the original

application (16 March 1999). Since this application now has the original priority date of the parent application a terminal disclaimer may be moot, however, if the Examiner still feels that a terminal disclaimer is necessary Applicants would be pleased to provide one.

C. Response to Claim Objections

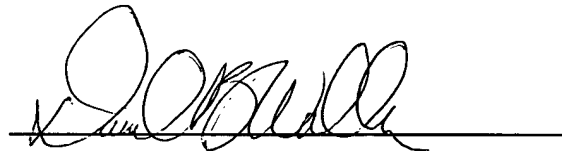
The Examiner objects to claims, 1, 2 and 11 for specific informalities. Claims 1 and 2 have been cancelled consequently the objections are moot. Applicant's have amended claim 11 to replace the term "fragment" with the terms "fragments" as requested by the Examiner. Consequently, Applicant's request that the Examiner remove this objection.

CONCLUSION

In view of the above arguments Applicant's have amended their claims and demonstrated that the invention as claimed satisfies the statutory requirements for patentability. Applicant's respectfully request that the Examiner issue an allowance of the claims.

Respectfully submitted,

Date: 23 November 2004



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